SEQUENCE LISTING

| <110> | SmithKline Beecham Corporation Lambert, Millard H Xu, Robert Wisely , Bruce Collins, Jon | | | | | | | | | | | | |
|----------------------------------|--|-----|--|--|--|--|--|--|--|--|--|--|--|
| <120> | CAR LIGAND-BINDING DOMAIN POLYPEPTIDE CO-CRYSTALLIZED WITH A LIGAND, AND METHODS OF DESIGNING LIGANDS THAT MODULATE CAR ACTIVITY | | | | | | | | | | | | |
| <130> | PR60235 | | | | | | | | | | | | |
| <150> <151> | 60/488,415 2003-07-18 | | | | | | | | | | | | |
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| | cctca tgaaaaatga ctgaccactg ctgggcagca ggagggatga taatcctaac | 120 | | | | | | | | | | | |
| | tcact ggcaactcct gagatcagag gaaaaccagc aacagcgtgg gagtttgggg | 180 | | | | | | | | | | | |
| | cattc cataccagat tctgtggcct gcaggtgaca tgctgcctaa gagaagcagg | 240 | | | | | | | | | | | |
| | gtgac agccacccca acacgtgacg tc atg gcc agt agg gaa gat gag Met Ala Ser Arg Glu Asp Glu 1 | 293 | | | | | | | | | | | |
| ctg a Leu A | igg aac tgt gtg gta tgt ggg gac caa gcc aca ggc tac cac ttt irg Asn Cys Val Val Cys Gly Asp Gln Ala Thr Gly Tyr His Phe 10 20 | 341 | | | | | | | | | | | |
| aat o Asn A | gcg ctg act tgt gag ggc tgc aag ggt ttc ttc agg aga aca gtc lla Leu Thr Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr Val 25 30 35 | 389 | | | | | | | | | | | |
| agc a Ser I 40 | aaa agc att ggt ccc acc tgc ccc ttt gct gga agc tgt gaa gtc Lys Ser Ile Gly Pro Thr Cys Pro Phe Ala Gly Ser Cys Glu Val 45 50 55 | 437 | | | | | | | | | | | |
| agc a Ser | aag act cag agg cgc cac tgc cca gcc tgc agg ttg cag aag tgc Lys Thr Gln Arg Arg His Cys Pro Ala Cys Arg Leu Gln Lys Cys 60 65 70 | 485 | | | | | | | | | | | |
| tta Leu | gat gct ggc atg agg aaa gac atg ata ctg tcg gca gaa gcc ctg Asp Ala Gly Met Arg Lys Asp Met Ile Leu Ser Ala Glu Ala Leu | 533 | | | | | | | | | | | |

| | | | | | | | | 00 | 2 | | | | 85 | | | | | |
|-------------------|-------------------|--------------------|--------------------|--------------------|----------------------|----------------------|--------------------|--------------------|--------------------|--------------------|--------------------|----------------------|-----------------|-------------------------|-------------------|--------------------|----------------|------|
| | | | 75 | | | | | 80 | | | | | | | | | | |
| gca Ala | ttg Leu | cgg Arg 90 | cga Arg | gca Ala | aag Lys | GIN | gcc Ala 95 | cag Gln | cgg Arg | cgg Arg | gca Ala | Cag Glr 100 | 1 61 | a a n T | ca hr | cct Pro | | 581 |
| gtg Val | caa Gln 105 | ctg Leu | agt Ser | aag Lys | gag Glu | caa Gln 110 | gaa Glu | gag Glu | ctg Leu | atc Ile | cgg Arg 11 |) ini | a ct r Le | c c | tg .eu | ggg Gly | | 629 |
| gcc Ala 120 | cac His | acc Thr | cgc Arg | cac His | atg Met 125 | ggc Gly | acc Thr | atg Met | ttt Phe | gaa Glu 130 | ווטו | tt Ph | t gt e va | 9 6 | ag 51n | ttt Phe 135 | | 677 |
| agg Arg | cct Pro | cca Pro | gct Ala | cat His 140 | ctg Leu | ttc Phe | atc Ile | cat His | cac His 145 | GII |) CC | c tt o Le | g co u Pi | ·O | acc Thr 150 | ctg Lei | } | 725 |
| gcc Ala | cct Pro | gtg Val | ctg Leu 155 | Pro | ctg Leu | gtc Val | aca Thr | cac His 160 | Phe | gca Ala | a ga a As | c at p Il | E ~: | ac <u>s</u> sn 65 | act Thr | tto Phe | 2 | 773 |
| atg Met | gta Val | ctg Leu 170 | ı Glr | gto Val | atc Ile | aag Lys | ttt Phe 175 | Thr | aag Lys | ga S As | c ct p Le | g co u Pr 18 | O A | tc al | ttc Phe | cg: | t g | 821 |
| tco Ser | cto Lei 185 | Pro | att | t gaa e Glu | gac J Asp | cag Gln 190 | Ile | tco Ser | cti Lei | t ct J Le | c aa u Ly 19 | ' S G | ja g ly A | ca la | gct Ala | gt Va | 9 | 869 |
| gaa G1: 200 | ıIle | tgi e Cy: | t ca s Hi | c ate | c gta e Va 20! | Lei | aat Asr | aco Thi | ac Th | t tt r Ph 21 | ie c | ys L | tc c eu G | aa iln | aca Thr | ca G1 21 | ** | 917 |
| aa Asi | tt n Ph | c ct e Le | c tg u Cy | c gg s G1 22 | g cc y Pro | t cti o Lei | cge Are | tao g Ty | c ac r Th 22 | L T | t g | aa g lu A | at g sp (| iga ily | gco Ala 230 | ית | jt 'g | 965 |
| gt Va | 9 gg 1 G1 | g tt y Ph | c ca e Gl 23 | n va | a ga 1 G1 | g tti u Pho | t tte | g ga u G1 24 | u Le | g ci | tc t eu P | tt c he H | 13 1 | ttc Phe 245 | ca ^r | t go s G | ga Iy | 1013 |
| ac Th | a ct r Le | a cg u Ar 25 | 'g L) | a ct /s Le | g ca u Gl | g ct n Le | c ca u G1 25 | חַ פו | g co u Pr | t g | ag t lu T | y, y | tg al 260 | ctc Leu | tt Le | g gg u A | ct la | 1061 |
| gc A1 | a Me | g gg et A | cc ct | tc t1 eu Ph | c to ne Se | t cc r Pr 27 | o As | c cg p Ar | g Pi | t g ro G | IY Y | tt a /al 1 !75 | icc Thr | cag Gln | ag Ar | a g g A | at sp | 1109 |
| ga G1 28 | ig at u I | tt ga le A | at c | ag ci ln Lo | tg ca eu G1 28 | ia ga In G1 35 | g ga u Gl | ig at | g g et A | ca c la L 2 | tg a eu 1 90 | hr i | ctg Leu | caa Gln | ag Se | ic ter T | ac yr 95 | 1157 |
| a! | tc a | ag g ys G | gc c ly G | in G | ag co ln Ai | ga ag rg Ai | ig co | ro A | ry A | at o sp A 05 | gg 1 krg 1 | ttt Phe | ctg Leu | tat Tyr | | eg a la L 10 | ag ys | 1205 |
| t L | tg c eu L | ta g eu G | ily L | tg c eu L 15 | tg g eu A | ct ga | ig C | eu A | gg a rg s 20 | gc a er : | itt [le | aat Asn | gag Glu | gce A1a 325 | <u>.</u> | ac g yr C | igg Sly | 1253 |

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1356

1416 1450

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| tac caa atc cag cac atc cag ggc ctg tct gcc atg atg ccg ctg ctc Tyr Gln Ile Gln His Ile Gln Gly Leu Ser Ala Met Met Pro Leu Leu 330 335 340 | 1301 |
| cag gag atc tgc agc tgaggccatg ctcacttcct tccccagctc acctggaaca Gln Glu Ile Cys Ser 345 | 1356 |
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| Gln Ala Thr Gly Tyr His Phe Asn Ala Leu Thr Cys Glu Gly Cys Lys 20 30 | |
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| Phe Ala Gly Ser Cys Glu Val Ser Lys Thr Gln Arg Arg His Cys Pro 50 60 | |
| Ala Cys Arg Leu Gln Lys Cys Leu Asp Ala Gly Met Arg Lys Asp Met 65 70 75 80 | |
| Ile Leu Ser Ala Glu Ala Leu Ala Leu Arg Arg Ala Lys Gln Ala Gln 85 90 95 | |
| Arg Arg Ala Gln Gln Thr Pro Val Gln Leu Ser Lys Glu Gln Glu Glu 100 105 | |
| Leu Ile Arg Thr Leu Leu Gly Ala His Thr Arg His Met Gly Thr Met 115 120 125 | |
| Phe Glu Gln Phe Val Gln Phe Arg Pro Pro Ala His Leu Phe Ile His 130 135 140 | |
| His Gln Pro Leu Pro Thr Leu Ala Pro Val Leu Pro Leu Val Thr His 145 150 150 | |
| Phe Ala Asp Ile Asn Thr Phe Met Val Leu Gln Val Ile Lys Phe Thr 165 170 175 | |

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Lys Asp Leu Pro Val Phe Arg Ser Leu Pro Ile Glu Asp Gln Ile Ser 180 185 190

Leu Leu Lys Gly Ala Ala Val Glu Ile Cys His Ile Val Leu Asn Thr 195 200 205

Thr Phe Cys Leu Gln Thr Gln Asn Phe Leu Cys Gly Pro Leu Arg Tyr 210 220

Thr Ile Glu Asp Gly Ala Arg Val Gly Phe Gln Val Glu Phe Leu Glu 225 230 235

Leu Leu Phe His Phe His Gly Thr Leu Arg Lys Leu Gln Leu Gln Glu 245 255

Pro Glu Tyr Val Leu Leu Ala Ala Met Ala Leu Phe Ser Pro Asp Arg 260 265 270

Pro Gly Val Thr Gln Arg Asp Glu Ile Asp Gln Leu Gln Glu Glu Met 275 280

Ala Leu Thr Leu Gln Ser Tyr Ile Lys Gly Gln Gln Arg Arg Pro Arg 290 295

Asp Arg Phe Leu Tyr Ala Lys Leu Leu Gly Leu Leu Ala Glu Leu Arg 305 310

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DNA

Homo sapiens

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ggg gcc cac acc cgc cac atg ggc acc atg ttt gaa cag ttt gtg cag

48

96

| | | | | | | | | | 5 | | | | | | | |
|-------------------|-------------------|----------------------|-----------------------|-------------------|-----------------------|-----------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-----------------------|-------------------|-------------------|-------------------|-----|
| Gly . | Ala | His | Thr 20 | Arg | His | Met | Gly | Thr 25 | | Phe | Glu | Gln | Phe 30 | ٧a٦ | Gln | |
| ttt Phe | agg Arg | cct Pro 35 | cca Pro | gct Ala | cat His | Leu | ttc Phe 40 | atc Ile | cat His | cac His | cag Gln | CCC Pro 45 | ttg Leu | CCC Pro | acc Thr | 144 |
| ctg Leu | gcc Ala 50 | cct Pro | gtg Val | ctg Leu | cct Pro | ctg Leu 55 | gtc Val | aca Thr | cac His | ttc Phe | gca Ala 60 | gac Asp | atc Ile | aac Asn | act Thr | 192 |
| ttc Phe 65 | atg Met | gta val | ctg Leu | caa Gln | gtc Val 70 | atc Ile | aag Lys | ttt Phe | act Thr | aag Lys 75 | gac Asp | ctg Leu | ccc Pro | gtc Val | ttc Phe 80 | 240 |
| cgt Arg | tcc Ser | ctg Leu | ccc Pro | att Ile 85 | gaa Glu | gac Asp | cag Gln | atc Ile | tcc ser 90 | ctt Leu | ctc Leu | aag Lys | gga Gly | gca Ala 95 | gct Ala | 288 |
| gtg val | gaa Glu | atc Ile | tgt Cys 100 | His | atc Ile | gta Val | ctc Leu | aat Asn 105 | acc Thr | act Thr | ttc Phe | tgt Cys | ctc Leu 110 | caa Gln | aca Thr | 336 |
| caa Gln | aac Asn | ttc Phe 115 | Leu | tgc Cys | 999 G1y | cct Pro | ctt Leu 120 | cgc Arg | tac Tyr | aca Thr | att Ile | gaa Glu 125 | gat Asp | gga Gly | gcc Ala | 384 |
| cgt Arg | gtg Val 130 | Gly | ttc Phe | cag Gln | gta Val | gag Glu 135 | ttt Phe | ttg Leu | gag Glu | ttg Leu | ctc Leu 140 | Pne | cac His | ttc Phe | cat His | 432 |
| gga Gly 145 | Thr | cta Leu | cga Arg | aaa Lys | ctg Leu 150 | Gln | ctc Leu | caa Gln | gag Glu | cct Pro 155 | GIU | tat Tyr | gtg | Ct C Leu | ttg Leu 160 | 480 |
| gct Ala | gco | ato Mei | gco Ala | cto Leu 165 | <u>ı</u> Phe | tct Ser | cct Pro | gac Asp | cga Arg 170 | Pro | gga Gly | a gtt / Val | acc Thr | cag Glr 175 | aga Arg | 528 |
| gat Asp | gaç Gli | ati Ile | t gat e Asp 180 | o G1r | g ctg n Leu | caa Gln | gag Gli | gag Glu 185 | ı Met | gca Ala | ctg Lei | g act u Thr | ctg Lei 190 | i Gir | a agc n Ser | 576 |
| tac Tyr | ate | c aag e Ly: 19 | s Gly | c caq y Gli | g cag n Glr | g cga n Arg | agg Arg 200 |) Pro | cgg Arg | gat J Asp | cg Ar | g tti g Phe 20: | e Lei | g tai | t gcg r Ala | 624 |
| aag Lys | tte Le 21 | ų Le | a gg u Gl | c cte | g cto u Lei | g gct u Ala 215 | a GII | g cto | c cgg u Arg | g age | c at r Il 22 | e ASI | t gag n Gli | g gc | c tac a Tyr | 672 |
| gg G1 22 | у Ту | c ca r Gl | a at n Il | c ca e Gl | g cad n Hi: 230 | s Ile | c ca e Gl | g gg n Gl | c cto y Lei | tc u se 23 | r Al | c ate | g at | g t | | 714 |
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| aaggag | caa | 69 |
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